mology department, so a diagnosis of HvCJD should be taken into consideration.

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Primary diffuse leptomeningeal melanomatosis: Description and recommendations

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ABSTRACT

Primary melanocytic disease of the central nervous system is a rarely encountered condition currently without consensus on treatment and lacking major guidelines for management. Understanding the nature of the disease and differentiating primary melanocytic disease from the much more commonly encountered secondary (metastatic) melanoma is important in identifying the condition and pursuing appropriate treatment.

1. Introduction

Melanocytic disease of the central nervous system is most often encountered in the setting of metastatic melanoma, a clearly pathological condition. Management strategies for this common presentation of melanoma are well established. Much more rarely encountered, and the focus of this review, is the clinical finding of primary melanocytic conditions of the central nervous system (CNS), which can present with symptoms or be incidentally detected without clinical correlate. Primary melanocytic disease of the CNS can be benign or extremely pathologic, or somewhere in between. Familiarity with the spectrum of melanocytic conditions of the CNS, their origins, and management of potential sequelae is important for clinicians who may encounter them.

Our goal in this review is to present a representative example of one of these conditions and its management, followed by a discussion into the origin of primary melanocytic conditions. We thoroughly describe multiple known primary melanocytic conditions, both benign and pathological, and their management strategies as currently described in the literature.

2. Case report

2.1. History and presentation

A 71-year-old female with a history of a non-invasive papillary bladder carcinoma developed left hemibody numbness, as well as mild left-sided weakness. She was referred to neurology for initial management. Further history revealed complaints of a recent onset of daily headaches, word-finding difficulty, and increasing difficulty with balance. Physical examination revealed bilateral 5/5 strength in upper and lower extremities with no pronator drift. Sensory examination showed diminished sensation to pain and light touch on the left side. Brain magnetic resonance imaging (MRI) demonstrated multiple nodular enhancing foci (Fig. 1). Initial management was frequent monitoring and serial MRIs. Several months after initial evaluation, the patient presented to the emergency room with new-onset confusion. Computed tomography (CT) revealed new-onset hydrocephalus, and a ventriculoperitoneal shunt was placed. Following recurrent confusion and new-onset diplopia, craniotomy for open biopsy was planned for tissue diagnosis.

2.2. Operation

In the operating room, a 3 × 3-cm bone flap was opened. Following dural opening, diffuse melanotic deposits were immedi-

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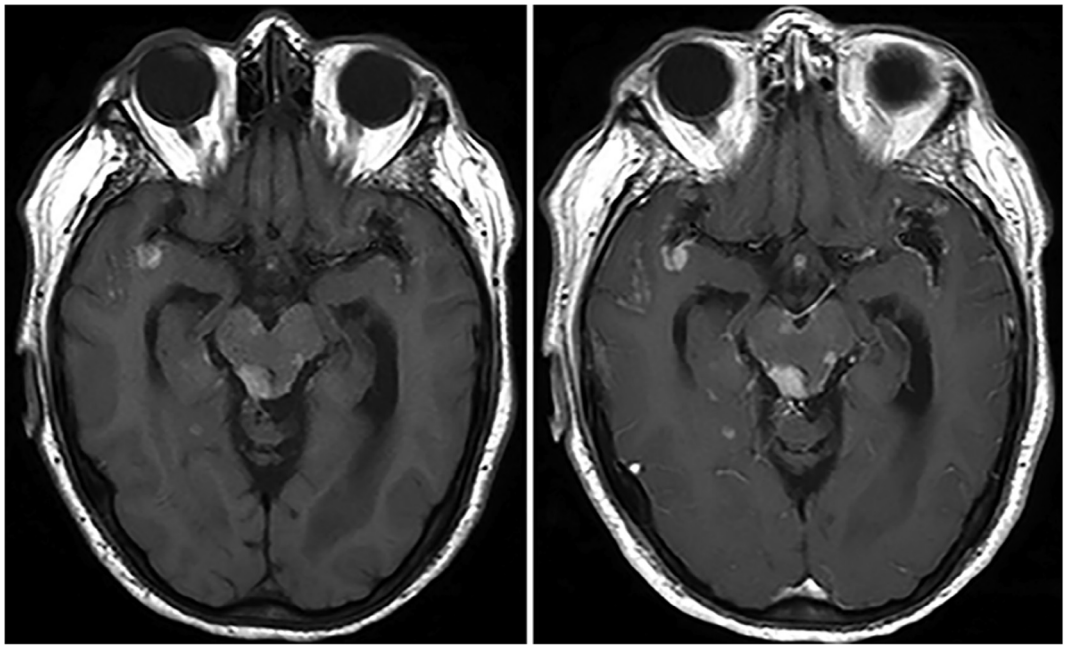

Fig. 1. Multiple intra-axial T1 hyperintense lesions visible in the bilateral insula, tectal region, cisterns, and along the midbrain. T1 sequences without (left) and with (right) contrast.

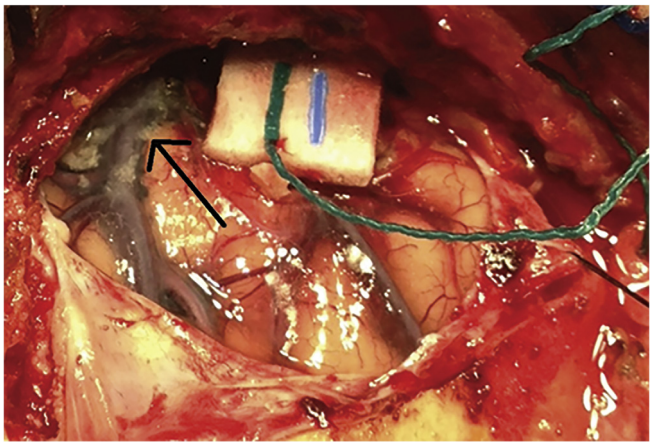

Fig. 2. Darkly pigmented melanotic deposits visible in the subarachnoid space after dura was opened and reflected.

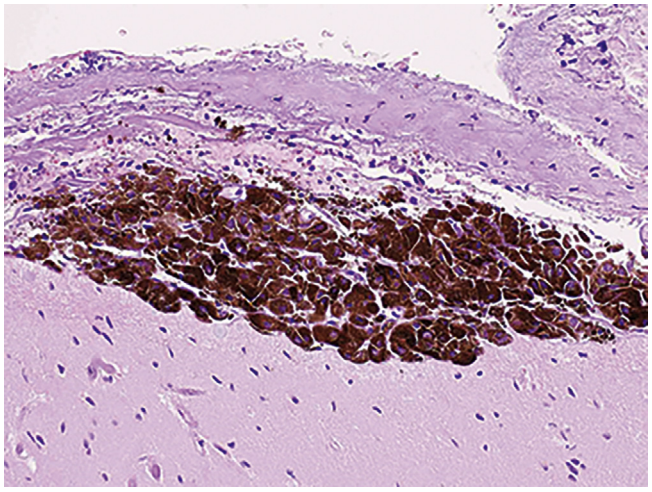

Fig. 3. A cluster of leptomeningeal cells contains numerous small, dark brown cytoplasmic melanin pigment granules. Most individual melanin granules are smaller than 3 μm in diameter. The dark pigment obscures nuclear details.

ately encountered in the subarachnoid space (Fig. 2). Several biopsies were collected for pathologic examination.

2.3. Pathologic findings

On histopathologic examination, the right temporal mass showed a leptomeningeal collection of large epithelioid cells that contained abundant darkly pigmented granules (Fig. 3). To reveal the cytologic detail of these cells, a permanganate bleaching procedure was performed (Fig. 4). The cells had round to ovoid nuclei with finely speckled chromatin, moderately-sized nucleoli, minimal cytologic atypia, and rare cytoplasmic inclusions. Mitotic activity was inconspicuous. The cells were positive for Melan A and were thus consistent with melanocytes. The proliferative index (Ki-67) was between 1 and 2%. Molecular testing for BRAF V600E/V600K and KIT mutations was negative. Depending upon the clinical context and extent of disease, these findings would be consistent with either melanocytoma or diffuse leptomeningeal melanomatosis. There was no evidence of parenchymal invasion or leptomeningeal spread and invasion into Virchow Robin spaces.

2.4. Postoperative course

Following her biopsy and diagnosis, the patient was referred to radiation and medical oncology for management of workup of metastatic melanoma. Dermatology evaluation revealed no skin lesions. Whole-body PET scan revealed no other areas of avid uptake. Workup of breast mass and fine-needle aspiration of thyroid nodule did not reveal other foci of disease. MRI of total spine was performed to assess for further central nervous system (CNS) involvement and revealed leptomeningeal involvement of the spinal cord and cauda equina. Given the absence of a primary mel-